REPORT OF A CASE IN WHICH THE FUSIFORM BACILLUS WAS ISOLATED FROM THE BLOOD STREAM.*

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In the year 1896 Vincent[1] described a fusiform bacillus associated with the spirilla which he believed to be the etiological agent of hospital gangrene. Vincent observed that the microorganisms associated with that disease were not unlike those found in certain cases of angina.

Two years previous to the work of Vincent, Plaut[2] reported five cases of angina caused by "Miller's bacillus," which was apparently the same organism as that described by Vincent. The organism is frequently referred to in the German literature as the Plaut-Vincent bacillus, while to the French and English writers it is known as the bacillus of Vincent or *B. fusiformis*. The earlier investigators were unsuccessful in their attempts to isolate the fusiform bacillus, and hence only certain morphological characters of the organism could be studied. Abel[3] was probably the first to cultivate this organism in the laboratory. He succeeded in growing *B. fusiformis* in a mixed culture with an unidentified diplococcus; after the second transplant, however, the fusiform bacillus was lost and further attempts to cultivate the organism were unfruitful.

Vincent cultivated *B. fusiformis* in the broth of Martin. In this medium the organism grew in long filaments, leaving the broth clear. This author observed that when transplanted from broth of Martin to media containing native albumin, such as ascitic fluid or blood serum, the organism would again resume its original fusiform shape. Zuber and Veillon[4] isolated an anaerobic organism from two cases of appendicitis which were probably identical with the bacillus of Plaut and Vincent. Lewkowicz[5] isolated the fusiform bacillus by growing it in the deeper layers of ascitic

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[1] *Ann. de l'Inst. Pasteur*, 1896, 10, p. 488.

[2] *Deutsch. med. Wchnschr.*, 1894, 20, p. 920.

[3] *Centralbl. f. Bakteriol.*, I Orig., 1898, 24, p. 1.

[4] *Arch. de méd. expér. et d'anat. path.*, 1898, 10, p. 517.

[5] *Bull. de l'Inst. Pasteur*, 1903, 1, p. 825.

glucose agar. Ellerman[1] was equally successful with his cultures on slant serum agar under pyrogallic acid and NaOH. Lewkowicz and Ellerman were unable to obtain cultures on any media except such as contained native albumin.

In this country *B. fusiformis* has been isolated and carefully described by Weaver and Tunnicliff;[2] these authors cultivated an organism under anaerobic conditions which corresponded morphologically and biologically with those described by the European writers. In 1900 Harris[3] isolated an anaerobic organism from a liver abscess which he christened *B. mortiferus*. The bacillus studied by Harris appears, however, to have been closely related to *B. fusiformis*.

MORPHOLOGY AND CULTURAL CHARACTERISTICS.

Preparations made from lesions containing *B. fusiformis* present a characteristic picture of long, slender, usually deep-staining rods associated with spirilla which ordinarily stain less intensely. The bacilli vary in length from 6 to 12 microns by 0.6 to 1 micron in breadth. They are spindle shaped, being swollen in the center and having distinctly pointed extremities. The bacilli stain unevenly, somewhat resembling the diphtheria bacilli in this respect. They are readily stained by any of the anilin dyes, and are gram-negative. The protoplasm of the bacilli seems to be concentrated in small masses or granules; these vary in number, according to the length of the bacillus, ranging from one to seven, the average being from two to four granules in each organism. The granules take the stain very deeply while the intervening space does not stain at all or is only very slightly tinged. Stained by the Romanowsky method the granules show distinct metachromasia.

The coexistence of the spirilla with bacilli has been the theme of much speculation; it has until quite recently been assumed that there was a symbiotic relation between two distinct microorganisms, the one being unable to thrive if the companion were absent. The cultivation of *B. fusiformis* by Abel, Vincent, Lewkowicz, Ellerman, and others would seem to disprove this theory, however, as these authors cultivated the bacillus separate from the spirillum. Tunnicliff[4] believes the spirillum represents another stage of the same organism, as she saw spirilla develop from the bacilli which were being cultivated on blood agar and ascitic agar.

The question whether or not *B. fusiformis* and the associated spirillum are motile is still an open question, if one is to judge from the literature. Bernheim[5] and Abel state that the bacillus has a slight vacillating movement. These authors made their observations on organisms taken direct from the buccal cavity, and it is therefore conceivable that the motility was due to some of the motile spirochetes normally found in the mouth. Carnot and Fourniet[6] and Plaut found the bacilli and spirilla to be motile when taken directly from the mouth, and the "spirochaetae" in culture retained their motility. On the other hand, Weaver, Tunnicliff, Lewkowicz, and Ellerman state that *B. fusiformis* (from the cultures) is non-motile. Tunnicliff later observed vibratory but no progressive motion from some of her cultures. Costa[7]

[1] *Centralbl. f. Bakteriol.*, I Orig., 1904, 37, p. 729.

[2] *Jour. Infect. Dis.*, 1907, 4, p. 8; *ibid.*, 1905, 2, p. 446.

[3] *Jour. Exper. Med.*, 1901, 6, p. 519.

[4] *Jour. Infect. Dis.*, 1911, 8, p. 316.

[5] *Centralbl. f. Bakteriol.*, I Orig., 1898, 23, p. 177.

[6] *Compt. rend. Soc. de biol.*, 1901, 53, p. 143.

[7] *Ibid.*, 1909, 67, p. 866.

examined pus containing *B. fusiformis* and found they were motile, provided they were not exposed to the air, but lost their motility upon coming under the influence of oxygen. The evidence is that no definite motility has been observed from cultures. Graupner[1] and Plaut and Veszprémi[2] have, by a special staining method, been able to demonstrate *B. fusiformis* to possess numerous peritrichic flagella. The presence of such flagella would naturally suggest that the organism is motile. Whether or not the organisms studied by these investigators were the same as those described by other writers must at present remain an open question.

The fusiform bacillus is a non-spore-bearer and does not form capsules. The organism under consideration is regarded by most authors as an obligate anaerobe. It will grow under aerobic conditions, however, after it has been cultured anaerobically for some generations, as the work of Weaver and Tunnicliff indicates. Abel, Vincent, Carnot, and Fourniet cultivated the organism aerobically in mixed cultures. When the organism is planted upon media containing native albumin and placed in oxygen-free environment, there appear small delicate colonies resembling those of the pneumococcus in from one to five days' incubation at 37° C. The colonies attain a size of from 1–2 mm. in diameter. After a few days' incubation the cultures are said to emit a foul, disagreeable odor. On glucose serum-agar Lewkowicz obtained a continuous undulate growth of a grayish hue. On ordinary slant agar Zuber and Veillon, and Weaver and Tunnicliff obtained a delicate growth, which, according to the latter authors, appeared along the line of inoculation, resembling a cloud on the surface of the medium. The development in gelatin at room temperature is very slow, and there is no liquefaction. Neither acid nor gas is formed on sugar media. In serum broth the organism grows in long filaments which settle, leaving a perfectly clear fluid.

PATHOGENICITY.

The fusiform bacillus is a normal inhabitant of the mouth (Mühlens,[3] Hartman, Miller[4]) and it has also been found on normal genitalia. In pathological conditions it has been found associated with a variety of necrotic lesions, such as ulceromembranous angina (Plaut, Vincent, and Bernheim) and ulcerative stomatitis (Perthes,[5] Ellerman, and others).

Vincent, Coyon,[6] and others have found it to be the cause of hospital gangrene. Veillon and Zuber observed that the organism may be a cause of appendicitis. It has likewise been found in gangrenous laryngitis (Bernheim and Pospischill[7]), empyema of the antrum of Highmore and fetid bronchitis (Silberschmidt[8]) associated with a metastatic abscess of the femur. Weaver, Tunnicliff, and others have found this organism in cases of noma. Quite recently Bevacqua[9] reports a case of pseudoelephantiasis in which he was able to demonstrate typical fusiform bacilli. Ellerman[10]

[1] *München. med. Wchnschr.*, 1902, 49, p. 727.

[2] *Centralbl. f. Bakteriol.*, 1907, 44, pp. 332, 408, 515, 648; *ibid.*, 45, p. 15.

[3] *Ztschr. f. Hyg. u. Infectionskrankh.*, 1906, 55, p. 81.

[4] *Die Mik. d. Mundhöhle*, Leipzig, 1892.

[5] *Arch. f. klin. Chir.*, 1899, 59, p. 111.

[6] *Ann. de l'Inst. Pasteur*, 1895, 9, p. 660.

[7] *Jahr. f. Kinderh.*, 1897, 46, p. 434.

[8] *Centralbl. f. Bakteriol.*, 1901, 30, p. 159.

[9] *Ibid.*, 1913, 68, p. 182.

[10] *Ztschr. f. Hyg. u. Infectionskrankh.*, 1907, 56, p. 453.

found *B. fusiformis* in the throats of 22 out of 38 cases of scarlet fever examined. Costa found the organism in a case of abscess of the kidney. Corbus[1] reports a number of cases of gangrenous balanitis probably due to this same organism.

In the preantiseptic days, cases of hospital gangrene were very common. Percy in a report issued from l'Hôtel-Dieu, Paris, states that 98 per cent of the wounds treated at that hospital were infected with the organism of hospital gangrene (cited by Vincent). During the European wars in the early part of the eighteenth century, hospital gangrene caused a very large mortality among the wounded. It was not uncommon for the surgeons attending such cases to become infected.

It is apparently very difficult, however, to produce an experimental infection. Vincent inoculated himself with the organisms which resulted only in an insignificant pustule. Gemy inoculated three persons with material from severe cases of hospital gangrene without success. It is to be assumed, therefore, that certain conditions must be fulfilled before an infection can take place. It is probable that the serum of a normal individual contains antibodies in the form of either lysins or opsonins by virtue of which the organisms are immediately destroyed. Inoculation experiments practiced upon animals have likewise met with but little success. Some investigators report that their animals succumbed with symptoms of toxemia a few hours after inoculation of large doses was made. Vincent produced a subcutaneous abscess in a cachectic rabbit by inoculating it with material from a patient suffering from hospital gangrene. The abscess thus produced evacuated itself spontaneously, on the sixth day following the inoculation, of a quantity of fetid pus containing the typical organisms. The same experiments performed upon healthy animals were negative. Silberschmidt produced abscesses in mice into which he had inoculated pus from a femoral abscess. The abscesses thus produced contained the fusiform bacilli in large numbers. Costa inoculated a guinea-pig with pus from a kidney abscess containing the organisms and thus succeeded in producing an abscess in the animal after an incubation period of several weeks.

In reviewing the work of the various investigators who have attempted to produce experimental lesions, one is struck by the

[1] *Jour. Am. Med. Assn.*, 1913, 60, p. 1769.

fact that the successful inoculations have almost invariably been made with material taken directly from the patient. Veszprémi, however, succeeded in producing lesions in animals by inoculating these with pure cultures. He invariably found other organisms associated with the fusiform bacillus in the lesions produced, and it is therefore difficult to determine which organism was responsible for the pathological changes.

By inoculating an animal with a quantity of pus containing the organisms it is not improbable that the ferments liberated by the disintegrating leukocytes produce local changes which favor the development of the infectious agent, either by virtue of the biochemical changes produced or by protecting the organisms from the influences of the antibodies. However, the possibility of the organism rapidly losing its virulence when cultivated artificially should not be overlooked.

In the light of Bail's[1] aggressin theory, the explanation would be very simple. According to this author, pathogenic bacteria have the property of forming substances which protect them from the action of the antibodies. He found, for instance, that pus from a streptococcic abscess, when heated sufficiently to destroy the bacteria, would produce no lesion if injected into an animal. If, however, an avirulent streptococcus was injected together with such material, the otherwise harmless organism became pathogenic. More recent investigations have shown that this same "aggressin action" may be obtained by the injection of bacterial filtrates. Further investigation of this problem is necessary, however, before a satisfactory explanation of the phenomenon can be offered.

CASE REPORT.

E. N. H., male, age 37, ticket collector at a theater, entered the Swedish Hospital, Minneapolis, September 30, 1912, on the service of Dr. S. P. Rees, giving the following history:

Was at work and apparently well up to three weeks previous to his admission, when he was taken with a sudden chill. After that he had to stop work occasionally because of a feeling of general malaise, altho he had no definite symptoms. He stated that his teeth were in very bad condition and that he suffered from night-sweats the week before entering the hospital.

[1] *Arch. f. Hyg.*, 1905, 52, p. 272; *Deutsch. med. Wchnschr.*, 1905, 31, p. 1788.

Physical examination revealed nothing abnormal with the exception of a hectic flush on cheeks, and a very severe pyorrhea alveolaris accompanied by an extremely foul breath. The condition in the mouth did not yield to ordinary antiseptic treatment, and a closer examination revealed extensive ulceration and necroses of the upper jaw.

During the stay in the hospital, patient ran a septic temperature with remissions in the morning to 98° F. and exacerbations in the afternoon to 104°. The pulse ranged between 100 and 135, but always regular; respiration 20 to 25.

Examination of the urine was negative except for a trace of albumin.

Leukocyte counts were as follows: October 2, 5,800; October 6, 2,400; October 12, 2,600.

Widal reaction on October 8 was negative, and Wassermann also negative.

Repeated examinations of the sputum did not reveal any tubercle bacilli. The laboratory reports of October 6 and 10 stated that diphtheria-like bacilli were present in the sputum. Subsequent more careful examinations revealed numerous spirilla and fusiform bacilli in the direct smears taken from the ulcerations in the mouth, and this led to a diagnosis of ulceration and gangrene due to infection with the fusiform bacillus.

Patient was in the hospital 28 days. At no time did he show any signs of any great discomfort or of pain. He developed no special symptoms up to a few days before his death, when he slowly sank into a stupor. Two days before his death, a blood culture was taken, the results of which will be described presently. Patient died on October 27, 1912, about seven weeks after the onset of the disease.

Abstract of autopsy protocol.—Body is well developed, but extremely emaciated. Embalming fluid is present in the body cavities. The skin around the nostrils and upper lip shows greenish discoloration. On reflecting the lips, the bone of the superior maxilla is blackened and necrotic. Probing shows destruction of the bone as far as the antrum of Highmore on the left side, and extending into the nasal cavities. The soft palate is necrotic, and the hard palate is rough and granular. There is a foul odor present, but no evidence of abscesses or gumma. The spleen is enormously increased in size, measuring 19 × 10 × 5 cm.

The findings of the other organs have no special import.

Blood culture.—The blood culture, made by aspirating the basilic vein 48 hours prior to exitus, was taken on plain agar, ascitic agar, and Loeffler's blood serum. The tubes were incubated for four days at 37° C. but no growth appeared. They were then incubated anaerobically in a Novy jar under hydrogen at 37° C. and after 48 hours the tubes of ascitic agar showed a scanty, rather dull, translucent, continuous growth. A few denser colonies, 1–2 mm., were scattered over the surface. The other media showed no growth.

Smears from these cultures showed a pure growth of fusiform bacilli which did not stain by Gram's method. Staining with Giemsa's stain diluted 1:10 for from 2 to 24 hours brought out one to two deeply staining bodies of a purplish-red color in each bacillus. The bacilli were distinctly canoe-shaped, being broadest at the middle and tapering to a point at both ends. Some were joined end-to-end in pairs, as if in the process of division. Generally, only one large granule was present in each of the paired bacilli, while most of the single bacilli contained two smaller granules. The organisms from the original culture were fairly uniform in size and shape. Some preparations showed small clumps of bacilli arranged radially about a central point.

In a general way, the morphology and staining of the bacilli corresponded almost exactly with the pure cultures described by Weaver and Tunnicliff.

Subcultures were planted on plain agar, ascitic broth, plain broth, ascitic agar, and Loeffler's blood serum. Tubes of each were incubated aerobically as well as anaerobically. At this time, no growth was obtained on the aerobic cultures. The anaerobic cultures showed growth on all but the plain agar; the best growth appeared on the ascitic agar.

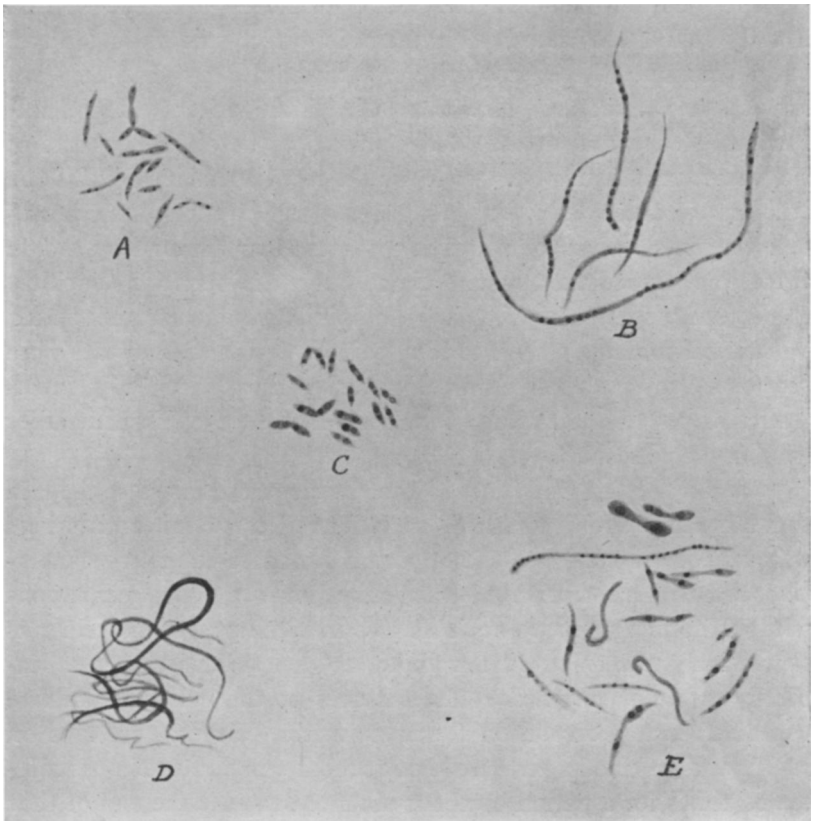

FIG. 1.—*A*, from an early culture on ascitic agar; *B*, from a blood agar culture; *C*, from an early culture; *D*, from blood agar showing spiral forms; *E*, some of the various forms the organism may assume in old cultures.

It was only after a number of anaerobic subcultures that we succeeded in growing the bacillus aerobically, and finally upon media containing no native albumins. But after this was ultimately accomplished, the cultures showed no less development under aerobic than under anaerobic conditions.

The morphology of the organisms from the original cultures and first transplantations was, as we have already said, fairly uniform. But with the subsequent

transplants marked polymorphism developed. This, just as Tunnicliff found, was especially noticeable when the transplantations were made on a medium upon which they had not previously grown. In the case of horse-blood agar, the organism showed a marked tendency to form spirals and long filaments. Some of these long filaments attained a length up to 100 microns and contained as many as 20 or 30 granules.

The relation between the fusiform bacilli and the spirilla usually found associated with them in direct smears is still an open question. The early writers, especially, deny that they are kin to one another. However, the later writers (Tunnicliff, Perthes, Neuof, and others) believe them to be different forms of the same organism. Our work would seem to confirm fully the opinions of these later authors. When the cultures from horse-blood agar, showing the spiral forms, were transplanted on ascitic agar, the transplants would show only the fusiform bacillus. Replanted on horse-blood agar, the spirals would often reappear.

Animal inoculations.—Rabbits, guinea-pigs, mice, and rats were inoculated intravenously, subcutaneously, intraperitoneally, intratesticularly, and into the anterior chamber of the eye, but invariably with negative results.

Viability.—The viability of the different strains described in the literature shows marked variation. Veszprémi and others were unable to cultivate the organism for more than two generations. Ellerman cultivated the organism for nine generations without noticing any appreciable loss in vitality. Our strain was successively transplanted for about 20 generations and the viability was fully retained. The cultures at the end of this time contained many involution forms, however. Several cultures on ascitic and on blood agar were kept at room temperature in paraffin-sealed tubes for a period of about six months. At the end of that time, transplants were made which were placed under aerobic as well as anaerobic conditions. Growth occurred only on the anaerobic cultures. From these we again succeeded in cultivating the organism aerobically.

Aside from the fact that our strain could be adapted, through successive transplants, to grow on media not containing native albumins, and under aerobic as well as under anaerobic conditions, the bacillus here described seems to be identical, culturally and

morphologically, with the fusiform bacillus described by other writers.

As far as we know, this is the first case on record in which the fusiform bacillus has been isolated from the blood stream. We therefore believed it to be of sufficient interest to warrant the presentation of this paper.

We wish to express our thanks to Dr. S. P. Rees for furnishing us the opportunity to study this case and for the history and hospital records.